Biodistribution and shedding analysis following treatment with RP1 oncolytic immunotherapy in the skin cancer patients from the IGNYTE clinical trial: implications for pharmacy and nursing staff.

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Background

• RP1 is a genetically modified herpes simplex virus type 1 (HSV-1) based oncolytic immunotherapy (OI) that selectively replicates in and kills tumors2,3,13.

• RP1 is under evaluation in a phase 1/2a open-label, multicenter, dose-escalation and dose-expansion trial evaluating the safety and efficacy of RP1 in combination with the anti-PD-1 antibody nivolumab in a range of tumor types (NCT02376734)2.

• RP1 is delivered intratumorally via injection into superficial lesions or deeper tumors using image guidance. Example handling of HSV-1-based OIs is shown in Figure 1. As the field of OIs continues to grow, the importance of understanding biosafety considerations is essential for pharmacy and nursing staff.

Patient and sample incidence of RP1 DNA detection

Table 1: Patient incidence of RP1 DNA detection

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>RP1 DNA positive</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>8/11 (72.7)</td>
<td>17/53 (32.1)</td>
</tr>
<tr>
<td>Urine</td>
<td>0/10 (0)</td>
<td>0/101 (0)</td>
</tr>
<tr>
<td>Mucosa</td>
<td>3/10 (30)</td>
<td>9/101 (9)</td>
</tr>
</tbody>
</table>

Figure 1. Example handling of HSV-1-oncolytic immunotherapies

Sample collection schema

Figure 2. Sample type and collection schedule

- Blood: The highest levels of RP1 DNA copy numbers were detectable in blood shortly (5 h) after injection. A subset of patients showed continued presence of RP1 DNA throughout the next 15 days (Table 1), highlighting RP1 replication in tumors (Figure 2).

- Urine: Throughout the 8 cycles, RP1 DNA was undetectable in urine samples. (Table 1 and 2).

- Mucosa: RP1 DNA was detectable at all sites examined throughout the study period, with highest levels seen in oral mucosa (Tables 1 and 2).

Infection site: The incidence of RP1 DNA was highest during Cycle 2 with approximately 20% of patients having detectable lesions at the injection site after 15 days post RP1 injection (Figure 6). During the safety follow-up period, RP1 DNA was only detected on the surface of infected lesions and not at any other sites (eg, blood, urine).

Figure 3. RP1 DNA levels in blood

Figure 5. RP1 DNA levels from the exterior dressing

Results

Table 2: Sample incidence of RP1 DNA detection

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>RP1 DNA positive</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>34/140 (24.3)</td>
<td>52/472 (11.0)</td>
</tr>
<tr>
<td>Urine</td>
<td>0/310 (0)</td>
<td>0/453 (0)</td>
</tr>
<tr>
<td>Mucosa</td>
<td>5/30 (16.7)</td>
<td>9/53 (17)</td>
</tr>
</tbody>
</table>

Figure 4. RP1 DNA levels at the site of injection

Figure 6. RP1 DNA levels from oral mucosa/saliva

Conclusions

• No infection RP1 virus was detected from any swab sample, only minimal RP1 DNA was concluded to be present.

• RP1 DNA was found less frequently on exterior dressing samples, suggesting that the dressing was an effective barrier.

• Overall, RP1 showed negligible potential for viral transmission to pharmacy staff and other caregivers, patients, and their families, with no evidence of transmission having been reported.

• At pharmacy sites, patient sample handling incorporates the use of viral oncolytic immunotherapies into patient care, biodistribution and shedding data will be important to evaluate during development of internal protocols for handling of these agents.

References


Table 1: Patient incidence of RP1 DNA detection

Table 2: Sample incidence of RP1 DNA detection

Figure adapted from: Robilotti E, et al. 2023;10:117832. © 2023 Robilotti, Zeitouni and Orloff.

Study Sponsor:

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Disclosure:

Oliver received payment from Genentech, Inc., Regeneron and Janssen for consultancy fees; he also received travel expenses related to attending meetings presented for marketing communications purposes.